THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today
(1) was not written for publication in a law journal and
(2) is not binding precedent of the Board.

Paper No. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte
MILTON G. SMITH

Appeal No. 1996-0605
Application 07/989,593

ON BRIEF

Before WINTERS, SPIEGEL, and ADAMS, Administrative Patent Judges,

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 8, 11, 14 and 23-32, which are all the claims pending in the application.

Claims 8 and 11 are illustrative of the subject matter on appeal and are reproduced below:

8. A method of delivering non-enzymatic antioxidants, comprising administering to a site in need thereof an effective amount of a free radical quenching composition comprising a liposome containing distributed within said liposome at least two members selected from the group consisting of beta-carotene, vitamin E, vitamin C, glutathione, and niacin, optionally at least one trace metal, and optionally a pharmaceutically acceptable carrier; wherein said administering is intravenously, intraarterially, intraperitoneally, subcutaneously, intramuscularly, intraarticularly, intracerebrally; intracerebellarly, intrabronchially, or intrathecally; whereby the level of said non-enzymatic antioxidants of said site is increased.

11. A method of increasing the level of antioxidants in a cell of a mammal, comprising administering to said mammal in need thereof an effective amount to increase the level of antioxidants in a cell of a mammal of a free radical quenching composition comprising a liposome containing distributed within said liposome at least two members selected from the group consisting of beta-carotene, vitamin E, vitamin C, glutathione, and niacin, optionally at least one trace metal, and optionally a pharmaceutically acceptable carrier; wherein said administering is intravenously, intraaterially, intraperitoneally, subcutaneously, intramuscularly, intraarticularly, intracerebrally, intracerebellarly intrabronchially, or intrathecally.

The references relied upon by the examiner are:

Lichtenberger 5,032,585 Jul. 16, 1991

Motoyam et al. (Motoyam) "Synergistic Inhibition of Oxidation in Dispersed Phosphatidylcholine Liposomes by a Combination of Vitamin and Cysteine" Archives of Biochemistry and Biophysics, Vol. 270, No. 2 (1989)

Ondrox "Unimed", Technical Bulletin, (1992)

GROUNDS OF REJECTION

Claims 8, 11, 14 and 23-32 are rejected under 35 U.S.C. § 103 as being unpatentable over Lichtenberger.

Claims 8, 11, 14 and 23-32[1] are rejected under 35 U.S.C. § 103 as being unpatentable over the advertisement for ONDROX (UNIMED) in combination with Motoyama.

DISCUSSION

In reaching our decision in this appeal, we have given careful consideration to the appellant's specification and claims, and to the respective positions articulated by the appellant and the examiner. We make reference to the Examiner's Answer (Answer)(Paper No. 22, mailed June 23, 1995) for the examiner's reasoning in support of the rejection. We further reference

[1] We note that page 7 of the Examiner's Answer (Paper No. 22, mailed June 23, 1995) does not identify the claims that pertain to this rejection. However, appellant's brief (Paper No. 20, received April 6, 1995) and the Final Rejection (Paper No. 11, mailed July 7, 1994) treat claims 8, 11, 14 and 23-32 as if they were rejected under this combination of references. Therefore, we will review the rejection of claims 8, 11, 14 and 23-32 under 35 U.S.C. § 103 as being unpatentable over the advertisement of ONDROX (UNIMED) in combination with Motoyama.

appellant's Brief (Paper No. 20, filed April 6, 1995), Corrections to Appeal Brief (Paper No. 21, received April 18, 1995) and Reply Brief (Paper No. 23, received August 23, 1995) for the appellant's arguments in favor of patentability.

CLAIM GROUPING:

At page 4 of the Brief, appellant states that claims 8 and 23-27 stand or fall together, and claims 11, 14 and 28-32 stand or fall together. However, we find no separate arguments as to the claims or designated groups as required by 37 CFR § 1.192(c)(5) (1994) (Claims stand or fall together "unless a statement is included that the rejected claims do not stand or fall together and, in the appropriate part or parts of the argument under paragraph (c)(6) of this section, appellant presents reasons as to why appellant considers the rejected claims to be separately patentable." (Emphasis added.)). Therefore, the claims on appeal are considered to stand or fall together with regard to each ground of rejection.

THE REJECTIONS UNDER 35 U.S.C. § 103:

Obviousness is a legal conclusion based on the underlying facts. Graham v. John Deere Co., 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966); Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1270, 20 USPQ2d 1746, 1750 (Fed. Cir. 1991); Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1566-68, 1 USPQ2d 1593, 1595-97 (Fed. Cir. 1987), cert. denied, 481 U.S. 1052 (1987).

LICHTENBERGER:

At page 4 of the Answer, the examiner states "Lichtenberger teaches liposomal compositions containing Copper and antioxidants E and C (note col. 7, lines 40-55; col. 8, lines 15-29; col. 15, lines 38-51; col. 23, lines 35-54[])]." In response to the examiner's position, appellant states at page 5 of the Brief that "[i]n fact, the reference notes that lipid preparations 'would have little or no luminal space as would a classical liposomal structure' (column 22, line 67 *et seq*)." Appellant therefore contends that "the reference teaches away from the claimed invention, since it is the lumenal space, the classical liposomal structure, in which Applicant's antioxidant composition rests." See, Brief, page 5. In addition, appellant provides the Stone Declaration to support this position. See, Stone Declaration (Paper No. 12, received October 17, 1994) paragraph 5, page 3, which states "the lack of luminal space would clearly preclude the ability to use this space to encapsulate chemical or enzymatic antioxidants."

The examiner responds to the Stone Declaration by stating ". . . fat soluble vitamins which are also claimed in the instant invention will not sequester in the aqueous interior of the liposomes, but would be within the lipid bilayer of the liposomes and thus, there is no issues of lack of luminal space." See, Answer, bridging paragraph of pages 6-7. However, Lichtenberger as relied on by the examiner discloses a liposomal composition containing vitamin E and C. See, Answer, page 4. In order to meet the limitations of the claims on appeal,

vitamin E and C must both be distributed within the liposome. See, e.g., Specification, Figure 8. While the examiner is correct in that the fat-soluble vitamin E (alpha-tocopherol) will not sequester in the aqueous interior of the liposome, vitamin C (ascorbic acid) certainly will. See, Specification, Figure 8. Since, as recognized by the examiner, Lichtenberger teaches liposomal compositions containing antioxidants E and C, we are confronted with the problem of where Lichtenberger's vitamin C is found if not in the aqueous interior of the liposome.

The Stone Declaration provides the answer. Page 2 of the Stone Declaration states, "[m]oreover, Lichtenberger at column 21, lines 65-68 suggests that the antioxidants would be added to the diluent and, therefore, water soluble vitamins would not be encapsulated into any liposomal preparations." Specifically, Lichtenberger discloses,

> However, for most applications it will generally be desirable to provide the lipids in the form of a colloidal or liposomal suspension of the selected composition in an pharmaceutically acceptable aueous diluent. While virtually an[y] pharmaceutically acceptable aqueous diluent may be employed, it has generally been found that a certain salt, for example in the form of isotonic saline has significant anti-ulcer activity. Further, small amounts of heavy metals (or other polyvalent cations) or anti-oxidant chemicals with the capability of scavenging free radicals can be added to the diluent to provide a lipid composition of greater anti-ulcer efficacy, stability and lumen-coating effectiveness.

See, Lichtenberger, column 21, lines 57- column 22, line 2.

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On the record before us, the examiner has not provided sufficient evidence to support a conclusion that the claimed subject matter would have been prima facie obvious within the meaning of 35 U.S.C. § 103 at the time of the invention. Lichtenberger does not teach a liposomal composition wherein both vitamin E and C are distributed with in the liposome as required by the claims on appeal. We, therefore, reverse the rejection of claims 8, 11, 14 and 23-32 under 35 U.S.C. § 103 over Lichtenberger.

ONDROX IN COMBINATION WITH MOTOYAMA:

The examiner states "UNIMED's advertisement on ONDROX shows the availability of mixtures of several antioxidants in a sustained release formulation. UNIMED teaches that the amounts of the antioxidants are theoretically synergistic (note the entire advertisement). UNIMED on cover page also teaches the reasons for the administration of antioxidants." See, Answer, pages 7-8, bridging paragraph. At page 8 of the Answer, the examiner states "Motoyama teaches the synergistic antioxidant effect of vitamins E and C in liposomes (note the abstract). Motoyama further discloses the antioxidant, glutathione. (page 656, column 1)." At page 8 of the Answer, the examiner concludes that::

> The use of liposomes taught by Motoyama in the teachings of UNIMED would have been obvious

> to one of ordinary skill in the art since liposomes are sustained delivery agents for drugs as well-known in the art and since Motoyama teaches a synergistic effect of the combination of antioxidants on oxidation even in liposome form.

In response to the examiner's position, appellant argues in the bridging paragraph of pages 18-19 of the Brief that "[t]he Examiner has not provided sufficient motivation for a person of ordinary skill in the art to modify a nutritional composition intended strictly for oral administration (Ondrox's tablet) with Motoyama's in vitro research composition, one in which a liposome contains one antioxidant and the aqueous medium contains another antioxidant)."

It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion or motivation to lead an inventor to combine those references. Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). Here the examiner states:

> The use of liposomes taught by Motoyama in the teachings of UNIMED would have been obvious to one of ordinary skill in the art since liposomes are sustained delivery agents for drugs as well-known in the art and since Motoyama teaches a synergistic effect of the combination of antioxidants on oxidation even in liposome form.

See, Answer, page 8. At page 11 of the Answer, the examiner states "[i]t is the examiner's position that both references teach synergistic effect of antioxidants

and both are concerned with sustained release systems." However, there is no suggestion in Motoyama that liposomes are "sustained release systems" or of using liposomes in a method of delivering non-enzymatic antioxidants, or a method of increasing the level of antioxidants in a cell of a mammal. The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On the record before us, the examiner has not provided sufficient evidence to support a conclusion that the claimed subject matter would have been prima facie obvious within the meaning of 35 U.S.C. § 103 at the time of the invention. We, therefore, reverse the rejection of claims 8, 11, 14 and23-32 under 35 U.S.C. § 103 over UNIMED in view of Motoyama.

OTHER ISSUES

We note the examiner's characterization of UNIMED at page 7 of the Answer, "UNIMED's advertisement on ONDROX shows the availability of mixtures of several antioxidants in a sustained release formulation . . . UNIMED on the cover page also teaches the reasons for the administration of antioxidants." We also note that liposomes were known in art at the time the invention was made to be drug delivery systems. See e.g., Iga et al., United States Patent No. 5,080,914. Upon return of this application, the examiner should take a step back and reevaluate patentability of the claimed invention in view of the art at the time the instant invention was made. If the examiner

believes, after this reevaluation, that the claims on appeal are unpatentable, he should issue an appropriate Office Action setting forth the rejection. In so doing, we urge the examiner to use the model set forth in MPEP § 706.02(j) for any rejection under 35 U.S.C. § 103. Adherence to this model will of necessity make the examiner examine the claims on appeal on an individual basis, using the correct legal standards.

SUMMARY

The rejection of claims 8, 11, 14 and 23-32 under 35 U.S.C. § 103 as being unpatentable over Lichtenberger is reversed. The rejection of claims 8, 11, 14 and 23-32 are rejected under 35 U.S.C. § 103 as being unpatentable over the advertisement for ONDROX (UNIMED) in combination with Motoyama is reversed.

REVERSED

Sherman D. Winters Administrative Patent Judge	))))) BOARD OF PATENT
Carol A. Spiegel Administrative Patent Judge	)) APPEALS AND)) INTERFERENCES
Donald E. Adams Administrative Patent Judge	))

DA/dm

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